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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/559,764	04/27/2000	Hans Jakob Flodgaard	5694.200-US	2707

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EXAMINER	
ROARK, JESSICA H	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/559,764	FLODGAARD ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-11,15-42 and 53-60* is/are pending in the application.

4a) Of the above claim(s) *7-11 and 15-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/10/03, is acknowledged.
Claims 1-6, 12-14 and 43-52 have been cancelled.
Claim 53 has been amended.
Claims 7-11, 15-42 and 53-60 are pending.

Claims 7-11 and 15-42 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. Applicant timely traversed the requirement in the Paper filed 11/20/00.

Claims 53-60 with respect to the elected species of SIRS (systemic inflammatory response syndrome) *are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 7/10/03.
The rejections of record can be found in the previous Office Actions (Paper Nos. 8, 12 and 16).

It is noted that New Grounds of Rejection are set forth herein.

3. Any rejection not reiterated below has been obviated by Applicant's amendment, filed 7/10/03, and removing the limitation requiring that the antibody bind an epitope of HBP which interacts with kininogen.

Claim Rejections – 35 U.S.C. §§ 102 and 103

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 53-55 and 60 are rejected under 35 U.S.C. 102(e) of as being anticipated by Oppenhelm et al. (US Pat. No. 5,837,247, of record, see entire document), as evidenced by Rasmussen et al. (FEBS Lett. 390:109-112 1996, of record, see entire document).

Applicant's arguments, filed 7/10/03, have been fully considered but have not been found convincing for the reasons of record.

As previously noted, Oppenhelm et al. teach a method for reducing or inhibiting an inflammatory disorder in a human subject comprising administering a monoclonal antibody antagonist of CAP37/HBP (see entire document; e.g., column 2, especially lines 57-67 and columns 9-10, especially bridging paragraph).

CAP37 and HBP are the same protein, as evidenced by Rasmussen et al. (e.g., "Introduction"), and would therefore inherently possess the functional and structural properties of HBP recited in instant claim 53.

Administration of what appears to be the same compound (an anti-HBP antibody) would inherently result in decrease in bradykinin release and the downstream effect of attenuation of alterations in endothelial cell permeability in a mammal, since the functional properties of the compound are inherent. Applicant is reminded that when a claim recites using an old composition or structure (e.g. an HBP-specific antibody) and the use is directed to a result or property of that composition or structure (e.g., effective to decrease release of bradykinin), then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant is further reminded that the courts have held that there is no requirement that those of ordinary skill in the art know of an inherent property, such as the inherent decrease in release of bradykinin in response to administering an antibody to HBP. See MPEP 2131.01(d) and MPEP 2112 - 2113 for case law on inherency

Systemic inflammatory response syndrome encompasses multiple inflammatory disorders; thus claim 60 is anticipated (see MPEP 2131.02).

Finally, no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitation of decreasing release of bradykinin and altering endothelial cell permeability would be an inherent property of a method comprising administering an anti-CAP37/HBP antibody to reduce or inhibit an inflammatory disorder. Further, it appears that any antibody that binds HBP and inhibits inflammation must bind the same epitope of HBP.

Applicant argues that because HBP contains a number of epitopes, Oppenhelm et al. can not anticipate the instant claims. However, Applicant provides no evidence that an antibody that bound HBP and had the function of reducing an inflammatory disorder would not inherently do so by decreasing the release of bradykinin.

Applicant is again invited to provide objective evidence that the antibodies taught by Oppenhelm et al. do not inherently possess the instantly recited properties.

However, until such time as some evidence is provided to support that the antibodies of Oppenhelm et al. do not inherently function to provide the same mechanism as that recited, the rejection of record is maintained.

It is noted that the amendment to claim 53 does not affect the rejection of record.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oppenhelm et al. (US Pat. No. 5,837,247, of record) as evidenced by Rasmussen et al. (FEBS Lett. 390:109-112 1996, of record); in view of Grunfield et al. (US Pat No. 5,660,826, of record).

Applicant's arguments, filed 7/10/03, have been fully considered but have not been found convincing for the reasons of record.

The claims are drawn to methods comprising administering specific dosages of an HBP/CAP37 antagonist wherein the antagonist is an antibody.

Oppenhelm et al. as evidenced by Rasmussen et al. have been discussed supra.

Oppenhelm et al. as evidenced by Rasmussen et al. teach a method of inhibiting inflammation by administering an antagonist anti-HBP antibody.

Oppenhelm et al. do not explicitly teach the dosage of administration of the antibody antagonist of HBP.

Grunfield et al. teach and claim a method comprising administering to a patient suffering from risk of systemic inflammatory response syndrome an effective amount of an antibody inhibitor wherein the antibody inhibitor is administered in the pharmaceutically effective amount of 1μg/kg to 10mg/kg (see entire document, especially claims 1 and 2). Grunfield et al. also teach that the dose is subject to a great deal of therapeutic discretion, and that higher doses may be needed (e.g., column 4, especially lines 23-37).

Given the teachings of Grunfield et al. with respect to dosages of administering antibodies for treating systemic inflammatory response syndrome conditions such as shock; it would have been obvious to the ordinary artisan at the time the invention was made to utilize similar dosages of antibodies to HBP, especially since the therapeutic use of anti-HBP antibodies taught by Oppenhelm et al. is for inhibiting inflammation. The ordinary artisan would have been motivated to utilize these similar dosages in light of the similarities of the therapeutic modality and the conditions treated. In addition, given these similarities, the ordinary artisan would have had a reasonable expectation that the effective dose of the antibody antagonist of HBP was similar to or encompassed by the range taught by Grunfield et al. Finally, the ordinary artisan would have been motivated to formulate the antibody composition in an amount of from about 10 mg to 1g per unit dosage in order to provide sufficient quantities of the antibody preparation in a reasonably compact dosing.

While many of the claim limitations are intrinsic to the method taught by Oppenhelm et al., the motivation to formulate the antibody at the recited concentration and administer it at the recited dosages is not affected by these intrinsic properties. Instead, the ordinary artisan would have been motivated based simply upon the need to formulate what appears to be the same product at a concentration and dosage appropriate to treat the disorder.

Applicant argues that there is no motivation to combine the teachings of the references because different therapeutics are used.

Although the specificity of the antibodies differ in the primary and secondary references, both therapeutics are antibodies which are administered for the treatment of inflammation. Thus the Examiner maintains that the teachings of Grunfield et al. do provide motivation and reasonable expectation of success with respect to the dose ranges at which an antibody should be administered for the treatment of inflammation.

Therefore, the Examiner maintains that the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

8. No claim allowed

9. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. This application contains claims 7-11 and 15-42 drawn to an invention nonelected with traverse in the paper filed 11/20/00. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is 703 872-9306.

Jessica Roark, Ph.D.
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Technology Center 1600
October 30, 2003

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